				to indicate how these 2 apparently counterdicting views should imbricate? *EFSA Response:* *Text in lines 1225-1226 has been changed as following: "Selective reporting can occur because non-significant results or unappealing significant results may not be published. Investigators should avoid the selective reporting of significant results and high-risk estimates. In this regard, standardization of reporting of epidemiological studies could help to reduce or avoid selective reporting. The STROBE statement and similar efforts are useful tools for this purpose."* *The text in line 1235 as been changed as following "Indeed, good studies may be dismissed during the formal quality assessment by the poor reporting of the information".*
110	Centre F Baclesse	FRA	4.1 Assessing and reporting the quality of epidemiological studies	• 1174-1175: Does the panel believe that the epidemiologic information on cigarette smoking and cancer, which was initially based on interview information, was inadequate for reaching a decision about tobacco hazards? • 1182-1185: I seriously doubt that it is "widely accepted" that 85% of biomedical research is wasted. This is an incredible charge, that is supported by a single publication of almost a decade ago. That fact that a group with such an important charge as this panel would make such a sweeping declaration is stunning. It may say more about the bias of this panel than the state of epidemiologic research on pesticides. • 1186-1189: It is correct that there are no special set of rules for evaluating the epidemiologic studies on pesticides. There are, however, written rules for evaluating epidemiologic data in general. These are taught in all the schools of public health and medical schools that have epidemiology training programs. Now I guess it could be that the faculty of these institutions are to ill-trained to perform this task or to adequately understand the strengths and weaknesses of epidemiology as well is this PPR Panel. This whole section implies that epidemiologists do not know how to report their work and that apparently most epidemiology studies do not even provide "a minimum set of information needed for a complete an clear account of what was done and what was found." What a stunning charge. Again apparently epidemiologists in the past used to provide adequate documentation because epidemiologic studies made major contributions to well accepted occupational and environmental causes of human disease. Obviously epidemiologists studying pesticides are too ill trained or two lazy to do it correctly. It is somewhat interesting that some epidemiologists engaged in studies of pesticides have conducted epidemiologic studies of other substances that apparently have met the needs of the scientific community. • 1189-1194: The idea that epidemiologic studies of pesticides have exposure assessment issues completely divorced from all other areas in epidemiology is simply wrong. Humans have complicated exposure patterns. This occurs whether they work with pesticides, in mines, in chemical plants, in steel mills, etc. • Table 1: I do not know what studies the PPR Panel is reading, but the epidemiology papers I read do these things. Perhaps the Panel could be more effective in improving the quality of work on pesticides by epidemiologists if they would provide more information on their survey the literature over the past several years and indicate the proportion of papers that DO NOT provide information on the factors in Table 1. Providing actual data would be a more scientific approach than simply implying that a large proportion of epidemiology studies of pesticides lack such information. *EFSA Response:* *Same text as comment #104 except last paragraph (see response elsewhere this report).*

111	Université de Bordeaux	FRA	4.1 Assessing and reporting the quality of epidemiological studies	• 1174-1175: Does the panel believe that the epidemiologic information on cigarette smoking and cancer, which was initially based on interview information, was inadequate for reaching a decision about tobacco hazards? • 1182-1185: I seriously doubt that it is "widely accepted" that 85% of biomedical research is wasted. This is an incredible charge, that is supported by a single publication of almost a decade ago. That fact that a group with such an important charge as this panel would make such a sweeping declaration is stunning. It may say more about the bias of this panel than the state of epidemiologic research on pesticides. • 1186-1189: It is correct that there are no special set of rules for evaluating the epidemiologic studies on pesticides. There are, however, written rules for evaluating epidemiologic data in general. These are taught in all the schools of public health and medical schools that have epidemiology training programs. Now I guess it could be that the faculty of these institutions are to ill-trained to perform this task or to adequately understand the strengths and weaknesses of epidemiology as well is this PPR Panel. This whole section implies that epidemiologists do not know how to report their work and that apparently most epidemiology studies do not even provide "a minimum set of information needed for a complete an clear account of what was done and what was found." What a stunning charge. Again apparently epidemiologists in the past used to provide adequate documentation because epidemiologic studies made major contributions to well accepted occupational and environmental causes of human disease. Obviously epidemiologists studying pesticides are too ill trained or two lazy to do it correctly. It is somewhat interesting that some epidemiologists engaged in studies of pesticides have conducted epidemiologic studies of other substances that apparently have met the needs of the scientific community. • 1189-1194: The idea that epidemiologic studies of pesticides have exposure assessment issues completely divorced from all other areas in epidemiology is simply wrong. Humans have complicated exposure patterns. This occurs whether they work with pesticides, in mines, in chemical plants, in steel mills, etc. • Table 1: I do not know what studies the PPR Panel is reading, but the epidemiology papers I read do these things. Perhaps the Panel could be more effective in improving the quality of work on pesticides by epidemiologists if they would provide more information on their survey the literature over the past several years and indicate the proportion of papers that DO NOT provide information on the factors in Table 1. Providing actual data would be a more scientific approach than simply implying that a large proportion of epidemiology studies of pesticides lack such information. *EFSA Response:* *Same text as comment #110.*
112	US EPA	USA	4.1 Assessing and reporting the quality of epidemiological studies	Table 1 Row Statistical methods (12) item (c). It is not just missing data, it is also data < LOD. *EFSA Response:* *Table 1 reports the list of STROBE Statement Items for observational studies where under row (12) item (c) it is only reported "explain how missing data were addressed". Data <LOD are not listed.*

113	Dept. Food Safety, Nutrition, Veterinary Public Health- Istituto Superiore di Sanità	ITA	4.1 Assessing and reporting the quality of epidemiological studies	1178-9: combined exposure to multiple chemicals may be considered a confounder from the strict standpoint of the use of epidemiological data for regulating one pesticide. On the other hand, a large part of human exposure scenarios involve the combined and concurrent exposure to several pesticides. Therefore, multiple exposures should be considered distinct from established "confounders" Suggested change: "adequately accounting for potentially confounding variables as well fror combined exposures to multiple pesticides" *EFSA Response:* *Agree (see also comments #30 and 205).*
114	LaKind Associates, LLC	USA	4.1 Assessing and reporting the quality of epidemiological studies	This document is a much-needed effort to highlight where environmental epidemiology research can be strengthened to support regulatory decision-making. Line 1200: The instrument we published in 2015 was updated in 2015 with slight modifications to improve clarity and transparency. I would be happy to send you a revised version. The cite is as follows (paper is Open Access): Environ Int. 2015 Jul;80:41-71. doi: 10.1016/j.envint.2015.03.015. Lessons learned from the application of BEES-C: Systematic assessment of study quality of epidemiologic research on BPA, neurodevelopment, and respiratory health. LaKind JS, Goodman M, Barr DB, Weisel CP, Schoeters G. This instrument was originally designed for assessment of study quality for epidemiology research that uses biomonitoring to assess exposure to short-lived chemicals. Since its publication, we have also used it for assessing study quality for persistent chemicals and also for environmental measures as its main elements are cross-cutting and are more broadly applicable. We are preparing a paper on this now and would be happy to share it when it is published. *EFSA Response:* *Agree. Text in lines 1199-1200 as been amended as following: "In addition, the Biomonitoring, Environmental Epidemiology, and Short-Lived Chemicals (BEES-C) instrument was developed to evaluate the quality of epidemiological research that use biomonitoring to assess short-lived chemicals (LaKind et al, 2015), but it can also be used for persistent chemicals and environmental measures as its main elements are cross-cutting and are more broadly applicable."* *Both papers from LaKind et al (2014 and 2015) has been referred to.*
115	Université de Bordeaux	FRA	4.1 Assessing and reporting the quality of epidemiological	1182-1185: I seriously doubt that it is "widely accepted" that 85% of biomedical research is wasted. This is an incredible charge, that is supported by a single publication of almost a decade ago. That fact that a group with such an important charge as this panel would make such a sweeping declaration is stunning. It may say more about the bias of this panel than the state of epidemiologic research on pesticides. *EFSA Response:* *Same text as comment #111.*

			studies	
116	Université de Bordeaux	FRA	4.1 Assessing and reporting the quality of epidemiological studies (see also 114)	1186-1189: It is correct that there are no special set of rules for evaluating the epidemiologic studies on pesticides. There are, however, written rules for evaluating epidemiologic data in general. These are taught in all the schools of public health and medical schools that have epidemiology training programs. Now I guess it could be that the faculty of these institutions are to ill-trained to perform this task or to adequately understand the strengths and weaknesses of epidemiology as well is this PPR Panel. This whole section implies that epidemiologists do not know how to report their work and that apparently most epidemiology studies do not even provide "a minimum set of information needed for a complete an clear account of what was done and what was found." What a stunning charge. Again apparently epidemiologists in the past used to provide adequate documentation because epidemiologic studies made major contributions to well accepted occupational and environmental causes of human disease. Obviously epidemiologists studying pesticides are too ill trained or two lazy to do it correctly. It is somewhat interesting that some epidemiologists engaged in studies of pesticides have conducted epidemiologic studies of other substances that apparently have met the needs of the scientific community. *EFSA Response:* *Same text as comments #104, 110 and 111.*
117	Université de Bordeaux	FRA	4.1 Assessing and reporting the quality of epidemiological studies (see also 114)	1189-1194: The idea that epidemiologic studies of pesticides have exposure assessment issues completely divorced from all other areas in epidemiology is simply wrong. Humans have complicated exposure patterns. This occurs whether they work with pesticides, in mines, in chemical plants, in steel mills, etc. *EFSA Response:* *Same text as comments #104, 110 and 111.*
118	Université de Bordeaux	FRA	4.1 Assessing and reporting the quality of epidemiological studies (see also 114)	Table 1: I do not know what studies the PPR Panel is reading, but the epidemiology papers I read do these things. Perhaps the Panel could be more effective in improving the quality of work on pesticides by epidemiologists if they would provide more information on their survey the literature over the past several years and indicate the proportion of papers that DO NOT provide information on the factors in Table 1. Providing actual data would be a more scientific approach than simply implying that a large proportion of epidemiology studies of pesticides lack such information. *EFSA Response:* *Same text as comments #104, 110 and 111.*

119	Defra Expert Committee on Pesticides on behalf of the Health & Safety Executive	GBR	4.2 Study design	At the individual study level substantial problems are reported with statistics - both application and interpretation. There are structural limitations that need to be clearly addressed. To give two examples: if using regression methods both response and explanatory variables need to be normally distributed; confidence limits in such analyses frequently dip below zero in some part of the range which is a biological impossibility. For many of these types of epidemiological studies Maximum Likelihood methods are more appropriate than Least Squares. Greater consideration of the a priori assumptions of statistical analyses at the design stage would seem to be desirable. *EFSA Response:* *The comment is well taken. The PPR Panel did try to convey that message in the report.* *A sentence was added in Section 4.2.*
120	personal	USA	4.3 Study populations	Line 2067-2068. The statement that "confounding by unmeasured factors associated with the exposure can never be fully excluded" seems to undercut the whole premise of utilizing epidemiological studies. In order to confound the relationship, there has to be a strong relationship between both the disease of interest and the exposure under study. A theoretical confounder is not an actual confounder and the document seems to indicate that associations are likely to due to some hypothetical factor that is both strongly associated with disease and exposure, but that has not been yet recognized as a risk factor for that disease. *EFSA Response:* *One limitation for the control of confounding in observational studies is that the data of all potential confounders may not be available since these studies usually use the data that have already been available. Thus, there are unknown confounders that were not measured. Hence, there is always a possibility to influence extraneous variables (unmeasured factors or unknown confounding) on the outcome of interest because of lack of comparability of two groups at baseline.* *The following text has been added to line 2068 to clarify the aforementioned sentence:* *"...fully excluded; however, a hypothetical confounder (yet unrecognized) may not be an actual confounder and has to be strongly associated with disease and exposure in order to have a meaningful effect on the risk (or effect size) estimate, which is not always the case."*
121	International Society for Environmental Epidemiology	POL	4.3 Study populations	**Comments on behalf of the Policy Committee, International Society for Environmental Epidemiology** The text is not a proposal strengthening of the use of epidemiology in risk assessment: the authors include what we recommend for sound epidemiology, but disregard practical and ethical limitations faced by epidemiological studies. They tend to favor weaker, ecologic, designs as case studies. Five areas of comment: • Epistemological. The authors favor toxicologic studies taking precedence over epidemiologic studies. This is contrary to how good science is built by the integration of knowledge that allows us to progressively get closer to the truth. They do not acknowledge weaknesses of in vivo experimental studies including biases, lack of representative human exposure patterns, incomplete ascertainment of outcomes or time to follow up, and several other problems. *EFSA Response:* *Some sentences have been included in the summary and in the Interpretation of the Terms of Reference to*